LAW OFFICES
HYMAN, PHELPS & MCNAMARA, P.C.

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MARC H. SHAPIRO
FRANCES K. WU
JEFFREY N. WASSERSTEIN
DAVID B. CLISSOLD
ROBERT T. ANGAROLA
(1945-1996)

700 THIRTEENTH STREET, N.W.
SUITE 1200
WASHINGTON, D. C. 20005-5929
(202) 737-5600
FACSIMILE
(202) 737-9329
www.hpm.com

JENNIFER B. DAVIS
KIRK L. DOBBINS*
OF COUNSEL

CASSANDRA A. SOLTIS
JOSEPHINE M. TORRENTE
MICHELLE L. BUTLER
ANNE MARIE MURPHY
PAUL L. FERRARI
LARRY K. HOUCK
DARA S. KATCHER*
KURT R. KARST
JULIE C. KLISH
CHRISTINE P BUMP*

*NOT ADMITTED IN DC

DIRECT DIAL (202) 737-4285

September 27, 2005

Division of Dockets Management [HFA-305]
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 2004N-0355

Dear Sir/Madam:

In its August 3, 2005 Federal Register Notice, the FDA invited written comments on the proposed scope of a planned Critical Path Initiative 2-day workshop. The stated purpose of this workshop is to explore approaches and potential obstacles to developing drugs, disease biomarkers, medical devices, and vaccines to prevent or reduce the risk of illness.

FDA is to be commended for holding this important workshop on approaches and potential obstacles to developing therapies to prevent and reduce the risk of illness. FDA appears to be contemplating break out sessions for cancer prevention issues, cardiovascular prevention issues and cerebrovascular prevention issues. In the Federal Register Notice, FDA asks what other conditions should be discussed. We recommend that a separate breakout session be held to discuss obstacles to development of new therapies for Alzheimer's disease and possible new approaches that may speed the development of new therapies for prevention or regression of this devastating disease.

2004N-0355

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2603 MAIN STREET
SUITE 760
IRVINE, CALIFORNIA 92614
(949) 553-7400
FAX: (949) 553-7433

4819 EMPEROR BOULEVARD
SUITE 400
DURHAM, NORTH CAROLINA 27703
(919) 313-4750
FAX: (919) 313-4751

In addition to a separate breakout session, we encourage the agency to consider selecting Alzheimer's disease as a model indication around which to focus the discussion of questions 3 through 8 on Day 1. In this way meeting participants will be able to have a more in-depth discussion of, for example, risk tolerance and regulatory hurdles.

Alzheimer's disease is a terminal and dehumanizing disease that affects not only the Alzheimer's patient, but also the patient's family and caregivers. The effects of Alzheimer's disease are devastating on an emotional, physical and very often financial level. The costs to society and our health care system are also extremely high and growing. By the year 2010, Alzheimer's disease will affect 5.6 million people in the U.S. (one in ten people over 65) -- as well as their families and caregivers. Government health care costs for Alzheimer's patients will increase 75 percent.

Dementia is the leading predictor of mortality in the elderly, and by the time Alzheimer's disease is definitively diagnosed, patients are already suffering significant neurological pathology. Available therapies provide modest symptomatic benefit but do not address the underlying cause of disease or its inevitable progression. Therefore, it is critically important to focus on approaches and potential obstacles to the acceleration of development for preventive and disease-modifying therapies in Alzheimer's disease. Merely looking for ways to accelerate approval timelines is not sufficient; all phases of development must be scrutinized.

The Federal Register Notice lists Alzheimer's disease, heart disease, diabetes and cancer as examples of the types of serious conditions for which preventive therapies are critically needed. Of these, Alzheimer's disease stands alone as the disease for which there are no examples of preventive or early diagnostic advances, and, in fact, is the only listed disease for which the Federal Register Notice does not provide examples of significant advances. It seems clear then that Alzheimer's disease should be included in the breakout sessions for Day 2 of FDA's workshop in addition to, or instead of, the diseases listed in the draft agenda.

The workshop can be used to identify potential surrogate markers that can be used to establish products for prevention or regression of disease. The quantum of evidence needed to establish a surrogate marker should be addressed to prevent the search for and proof of the marker becoming more onerous than conducting standard studies that are used to demonstrate symptomatic relief. Historically, tools such as the Alzheimer's Disease Assessment Scale (ADAS-cog) or the Clinician's Interview Based Impression of Change (CIBIC) have been used to establish efficacy. There should be discussion and consideration of other assessment tools that might be more sensitive to changes in a patient's cognitive performance and that might speed the introduction of new and

promising therapies. Safety standards and risk prevention programs might be discussed. Given the debilitating nature of Alzheimer's disease, new approaches are in order.

We must recognize that Alzheimer's disease is debilitating, dehumanizing, and fatal. We encourage policy makers and regulators to make the advancement of promising Alzheimer's disease therapies a high priority, and help bring transforming therapies to patients, providers and families by the beginning of the next decade.

Sincerely,

Roger C. Thies

RCT/dh